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KLARQUIST SPARKMAN, LLP
121 SW SALMON STREET
SUITE 1600
PORTLAND, OR 97204

EXAMINER	
DOWELL, PAUL THOMAS	
ART UNIT	**PAPER NUMBER**
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/517,154	MORISHITA ET AL.	
	Examiner	Art Unit	
	Paul Dowell	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/7/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment of 12/06/2004 is acknowledged and in that ammendement Claims 9 and 10 have been cancelled. Claims 1-8, 11 are pending and are under examination in the instant office action.

Priority

The instant application was filed on 7/11/2005, which is a § 371 U.S. national stage of PCT/JP03/07004, filed on June 3, 2003, and claims the benefit of Japanese Patent Application No. 2002-165437, filed June 6, 2002.

Information Disclosure Statement

The information disclosure statement filed 3/7/2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. No copy of Ishida et al was in the file of record. It has been placed in the application file, but the document of Ishida et al was not considered and a line has been drawn through the listing of said document.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA

1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 6-7, 11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of **U.S. Patent No. 6,936,594 B1, Issued 8/30/2005**. Although the conflicting claims are not identical, they are not patentably distinct from each other because said claims of the instant application and claim 1 of the cited patent are both drawn to a method of treating cerebrovascular disorders comprising administration of a nucleic acid encoding hepatocyte growth factor wherein said nucleic acid is in the form of HVJ-liposomes.

The claims of the present application and the cited patent differ one from the other in that the instant claims may comprise a nucleic acid encoding a protein effective as a hepatocyte growth factor while the claims of the cited patent may further comprise a nucleic acid encoding vascular endothelial growth factor, however, both the claims of the instant application and the claims of the cited patent encompass a hepatocyte growth factor gene alone in the form of HVJ-liposome. It is noted that the product claims of the instant application (claims 1-4) are required for the method claimed in the cited patent. Accordingly, the inventions as claimed are co-extensive.

Claim Objections

Claims 4, 5, 8 and 11 are objected to because the abbreviation "HVJ" should be defined the first time it appears in the Claims.

Specification

The abstract of the disclosure is objected to because "TTC" should be spelled out the first time it appears in the specification. It is noted that the term "TTC" is present on page 17, line 24 and on page 20, line 14. Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-8, 11 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1 and 8 recite, "a nucleic acid" or "the nucleic acid" and when given broadest reasonable interpretation read on a nucleic acid that is a product of nature. Products of nature are considered non-statutory subject matter. Substituting "an isolated nucleic acid" for both "a nucleic acid" and "the nucleic acid" may overcome this rejection. It is noted that Claims 2-7, 11 depend from Claim 1 and therefore are likewise rejected under 35 U.S.C. 101.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written description

Claims 1-8, 11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is drawn to an agent comprising a nucleic acid encoding a protein effective as a hepatocyte growth factor and a method of treatment comprising introduction of said agent.

When Claims 1 is analyzed in light of the specification, the agent (i.e. "a nucleic acid encoding a protein effective as a hepatocyte growth factor") encompasses any nucleic acid that "has practically the same function as HGF" (see page 9, line 9 of the specification) and as such would encompass a large number of nucleic acid molecules that have divergent structure and function. However, the specification discloses only an HGF cDNA of human origin (page 18, line 10 of the specification).

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, the HGF cDNA of human origin is the

only species of nucleic acids encoding a protein effective as a hepatocyte growth factor whose complete structure is disclosed. The art of record at the time of the invention recognized a large number of HGF genes present in mammals, avians and amphibians that function as growth regulators **(**for example see Ghrerdi et al, **Ciba Foundation Symposium, 212:24-45, Abstract only)**. However, the specification does not provide any disclosure about the structure of proteins in relation to their effectiveness as hepatocyte growth factors. Further, the specification does not provide any disclosure as to what would have been the complete structure of a sufficient number of species of the claimed genus that would have been representative of the entire genus of nucleic acids encoding a protein effective as a hepatocyte growth factor.

Next, then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. other than nucleic acid sequence), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, the only identifying characteristic of nucleic acids encoding a protein effective as a hepatocyte growth factor is that they encode a protein effective as a hepatocyte growth factor. Such limitations cannot be identifying characteristics for the claimed diverse genus of nucleic acid molecules because all members of the claimed genus will have those functional characteristics.

The invention of Claims 2-8, 11 require the invention of Claim 1 and therefore are likewise rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Applicants' attention is directed to the decision in *In re Shokal*, 113 USPQ 283 (CCPA 1957) wherein is stated:

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

Further, Applicant's attention is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

In summary the specification does not describe the complete structure of a representative number of species of the large genus of nucleic acids encoding a protein effective as a hepatocyte growth factor. Further, the specification does not sufficiently describe a representative number of species of the the large genus of nucleic acids encoding a protein effective as a hepatocyte growth factor by other relevant identifying characteristics, specific features and functional attributes that would distinguish different members of the claimed genus. The specification discloses only an HGF cDNA of human origin as a representative of nucleic acids encoding proteins effective as hepatocyte growth factors. The limited information provided in the specification is not deemed sufficient to reasonably convey to one skilled in the art that Applicant was in possession of the genus at the time the application was filed. Thus, it is concluded that the written description requirement is not satisfied for the claimed genus.

Enablement

Claims 1-8, 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

an agent for reducing the infarcted area of a cerebral infarction, wherein said agent comprises a nucleic acid encoding a hepatocyte growth factor protein and;

a method for reducing the infarcted area of a cerebral infarction comprising administration of a nucleic acid encoding a hepatocyte growth factor protein by direct injection into the subarachnoid space of a subject prior to the occurrence of said cerebral infarction, wherein said method results in a reduction of the infarcted area,

does not reasonably provide enablement for an agent for treating or preventing any cerebrovascular disorder, wherein the agent comprises any nucleic acid encoding a protein effective as a hepatocyte growth factor and;

does not reasonably provide enablement for a method of treating or preventing any cerebrovascular disorder comprising administration of any nucleic acid encoding a protein effective as a hepatocyte growth factor by any route of administration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When

determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)).

Furthermore, the USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

The claimed invention is drawn to an agent for treating or preventing a cerebrovascular disorder, wherein the agent comprises a nucleic acid encoding a protein effective as a hepatocyte growth factor; and a method for treating or preventing a cerebrovascular disorder, wherein the method comprises introduction of said agent. Given broadest reasonable interpretation, the claimed invention encompasses an agent comprising any nucleic acid encoding a protein effective as a hepatocyte growth factor. However, the specification discloses only a hepatocyte growth factor (HGF) cDNA of human origin as a nucleic acid encoding a protein effective as a HGF (page 18, line 10). The specification discloses that it is possible to determine if a protein has HGF activity by investigating the effect of said proteins on the *in vitro* proliferation of hepatic

parenchymal cells (page 10, lines 27-33). The specification discloses that a nucleic acid encoding HGF of human origin reduces the infarcted area of a cerebral infarction when injected directly into the subarachnoid space of a rat prior to inducing said cerebral infarction by carotid artery occlusion (Working example 3, page 18-19). However, the specification and the art of record at the time of the invention provide no evidence that there is any correlation between the ability of a protein to stimulate proliferation of hepatic parenchymal cells and the ability of said protein to modulate cerebral infarctions. Therefore, an artisan would experience undue experimentation to practice the claimed invention with any nucleic acid encoding a protein effective as a hepatocyte growth factor because an artisan would not know how to choose any nucleic acid encoding a protein effective as a hepatocyte growth factor that would be operative in the claimed invention with any degree of predictability.

The claimed invention is drawn to an agent for treating or preventing a cerebrovascular disorder, wherein the agent comprises a nucleic acid encoding a protein effective as a hepatocyte growth factor and a method for treating or preventing a cerebrovascular disorder, wherein the method comprises introduction of said agent. Given broadest reasonable interpretation, the claimed invention encompasses a method for treating or preventing any cerebrovascular disorder by any route of administration.

Regarding any cerebrovascular disorder, the specification defines cerebrovascular disorders as any condition in which blood flow to the brain is inhibited (page 16, line 5) and that inhibited blood flow is not limited to that caused by disease (page 16, line 8), for example from an injured blood vessel due to a wound (page 16,

lines 10-11). The specification discloses that a nucleic acid encoding HGF of human origin reduces the infarcted area of a cerebral infarction when injected directly into the subarachnoid space of a rat prior to inducing said cerebral infarction, wherein said cerebral infarction is induced by carotid artery occlusion (Working example 3, page 18-19). However, it is not clear how the claimed method would be used to treat or prevent cerebrovascular disorders that do not result in cerebral infarctions because the specification discloses only a method of treatment that is effective in reducing the infarcted area of a cerebral infarction. Therefore, an artisan would experience undue experimentation to practice the claimed invention to treat any cerebrovascular disorder, in particular, those cerebrovascular disorders that do not result in a cerebral infarction, because an artisan could not know, with any degree of predictability, which cerebrovascular disorders would be treatable other than those cerebrovascular disorders resulting in a cerebral infarction.

Regarding any route of administration, the specification provides a laundry list of methods for transferring genes into cells including lipofection methods, liposomes, HVJ-liposomes, particle guns and positively charged polymers, for example (page 11, lines 19-29). The specification further recites that such methods can be used to deliver genes either *in vivo* or *ex vivo* (page 13, lines 24-27). However, the only route of administration taught by the specification is direct injection into the subarachnoid space of rat brain via cisternal administration (Working Example 3, page 18). The Claims recite a method comprising a step of "introduction of the agent" and given broadest reasonable interpretation read on any route of administration. The art of gene therapy in general is

unpredictable and delivery of genes to the brain is further complicated by the presence of the blood-brain barrier. For example, at the time of the invention, Pardridge **(Japanese Journal of Pharmacology, 87:97-103, 2001)** recognized that many gene therapy vectors, including cationic liposomes and viral vectors, cannot penetrate the blood-brain barrier thus necessitating direct deliver into the brain (page 101, col. 1, paragr. 1, lines 1-6). The art of record continues to recognize the technical hurdles of gene therapy directed to the brain. For example, de Lima et al **(Current Drug Targets for CNS Neurological Disorders, 4:453-465, 2005)** recognize that the blood-brain barrier continues to be an impediment to systemically delivered macromolecules with therapeutic activity (see Abstract). Therefore, an artisan would experience undue experimentation to practice the claimed method of treating a cerebrovascular disorder by any route of administration because of the unpredictability of gene therapy in general and the additional unpredictability of delivering genes to the brain.

Further, the Claims recite a method for treating or preventing a cerebrovascular disorder. Working Example 3 (page 18)/ Figure 4 discloses that a nucleic acid encoding HGF of human origin reduces the infarcted area of a cerebral infarction when injected directly into the subarachnoid space of a rat prior to inducing said cerebral infarction, wherein said cerebral infarction is induced by carotid artery occlusion. However, the specification provides no specific guidance as to how said method would be used for preventing cerebrovascular disorders in a human population, for example. In particular, how would an artisan identify the relevant patients in need of preventative treatment for said cerebrovascular disorders? The specification provides no specific guidance as to

how an artisan would identify a population of subjects in need of preventative treatment with the method of the claimed invention. Therefore, an artisan would experience undue experimentation to practice the claimed method of preventing a cerebrovascular disorder because an artisan would not know, with any degree of predictability, which patients are in need of preventative treatment for said cerebrovascular disorders.

The specification as filed does not provide sufficient guidance to make an agent for treating or preventing any cerebrovascular disorder, wherein the agent comprises any nucleic acid encoding a protein effective as a hepatocyte growth factor and does not provide sufficient guidance for a method of treating or preventing any cerebrovascular disorder comprising administration of any nucleic acid encoding a protein effective as a hepatocyte growth factor by any route of administration. An artisan of skill would have required extensive experimentation to practice the claimed invention commensurate with the scope of the claims. Such experimentation will be undue because of the unpredictability of practicing the claimed method using any nucleic acid encoding a protein effective as a hepatocyte growth factor, the unpredictability of gene therapy in general and the unpredictability of preventing cerebrovascular disease in a population. The specification does not provide sufficient guidance to address these issues for an artisan to practice the claimed invention.

Therefore, limiting the scope of the claimed invention to:

an agent for reducing the infarcted area of a cerebral infarction, wherein said agent comprises a nucleic acid encoding a hepatocyte growth factor protein and;

a method for reducing the infarcted area of a cerebral infarction comprising administration of said nucleic acid encoding a hepatocyte growth factor protein by direct injection into the subarachnoid space of a subject, wherein said method results in a reduction of the infarcted area, is proper.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "effective" in Claim 1 is a relative term which renders the claim indefinite. The term "effective" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The specification on page 10, lines 27-33 discloses how to determine that a nucleic acid encodes a protein effective as a hepatocyte growth factor and recites, "investigating the effect of these proteins on the *in vitro* proliferation of hepatic parenchymal cells". However, the specification does not define what would be considered "effective" and does not provide a standard for ascertaining the requisite degree of effectiveness.

Claims 6-8, 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is drawn to a method of treating or preventing a cerebrovascular disorder, wherein the method comprises introduction of the agent of claim 1, however, claim 6 does not recite any positive step which clearly relates back to the preamble. It is unclear how introduction of said agent relates to the treatment of cerebrovascular disorders or whether the goal of said method has been resolved. Claims 7, 8 and 11 depend from claim 6 and therefore are likewise rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 6, 7, 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Morishita et al **(Australian Patent Application No. 200073148 B2, published 4/24/2001, now Patent No. 774990)**.

Claims 1-4 are drawn to an agent for treating or preventing a cerebrovascular disorder comprising a nucleic acid encoding a protein effective as a hepatocyte growth factor and Claims 6, 7, 11 are drawn to a method of treating or preventing a cerebrovascular disorder comprising introduction of said agent. Claim 3 further limits said agent, wherein said agent is in the form of a tablet, pill, sugar-coated tablet, capsule, liquid, gel, ointment, syrup, slurry or suspension. Claims 2 and 7 further limit said cerebrovascular disorder to a cerebral infarction; Claims 4 and 11 further limit said agent, wherein said agent further comprises viral envelope vectors, liposomes, HVJ-liposomes, receptor-mediated gene transfer, using a particle gun, direct introduction of naked nucleic acid, introduction using a cationic polymer, or combinations of two or more thereof.

Morishita et al teaches an agent for cerebrovascular disorders comprising hepatoctye growth factor as an active ingredient wherein said cerebrovascular disorders comprise a cerebral infarction (Claims 1 and 2). Morishita et al teaches said agent further comprising a liquid (page 25, line 7), viral envelope vector (page 23, lines 20-22), an internal type liposome, an electrostatic type liposome, an HVJ-liposome or improved HVJ-liposome and a positively charged (i.e. cationic) polymer (page 22, lines 6-18).

Morishita et al also teaches a therapeutic or preventive method for cerebrovascular disorders comprising introducing into a human subject a nucleic acid encoding hepatocyte growth factor (Claim 13). Morishita et al teaches said method to treat cerebral infarctions (page 19, line 8). Further, Morishita et al teaches said method wherein the introduction of the nucleic acid encoding hepatocyte growth factor

comprises introducing the nucleic acid by viral envelope vectors (page 23, lines 20-22), internal type liposomes, electrostatic type liposomes, HVJ-liposomes or improved HVJ-liposomes, receptor-mediated gene transfer, transfer of nucleic acid using a particle gun, direct introduction of naked DNA and introduction with positively charged (i.e. cationic) polymers (page 22, lines 6-18). Thus, Morishita et al anticipates the claimed invention.

It is noted that the use of a product for a particular purpose is not afforded patentable weight in a product claim where the body of the claim does not depend on the preamble for completeness but, instead, the structural limitations are able to stand alone. The MPEP recites (see 2111.02), "If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction. Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999).

Claims 1-4, 6-7, 11are rejected under 35 U.S.C. 102(e) as being anticipated by Morishita et al **(U.S. Patent No. 6,936,594 B1, Issued 8/30/2005)**.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in

the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1-4, 6-7, 11 of the instant application are drawn to an agent comprising a nucleic acid encoding a protein effective as a hepatocyte growth factor in the form of HVJ-liposome and a method of treating cerebrovascular disorders comprising administration of a nucleic acid encoding a protein effective as a hepatocyte growth factor in the form of HVJ-liposome.

Morishita teaches a method of treating cerebrovascular disorders comprising administration of a nucleic acid encoding hepatocyte growth factor and/or a nucleic acid encoding vascular endothelial growth factor in the form of HVJ-liposome (Claim 1).

The claims of the present application and the cited patent differ one from the other in that the instant claims may comprise a nucleic acid encoding a protein effective as a hepatocyte growth factor while the claims of the cited patent may further comprise a nucleic acid encoding vascular endothelial growth factor, however, both the claims of the instant application and the claims of the cited patent encompass a hepatocyte growth factor gene alone in the form of HVJ-liposome. It is noted that the product claims of the instant application (claims 1-4) are required for the method claimed in the cited patent. Thus, Morishita anticipates the claimed invention of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morishita et al **(Australian Patent Application No. 200073148 B2, published 4/24/2001, now Patent No. 774990)** in view of Ramani et al **(Proceedings of the National Academy of Science, USA, 95:11886-11890, 1998)**.

Claim 5 is drawn to an agent for treating or preventing a cerebrovascular disorder comprising a nucleic acid encoding a protein effective as a hepatocyte growth factor wherein the agent further comprises an HVJ-envelope. Claim 8 is drawn to a method of treating or preventing a cerebrovascular disorder comprising introduction of said agent.

Morishita et al teaches a therapeutic or preventive method for cerebrovascular disorders comprising introducing into a human subject a nucleic acid encoding hepatocyte growth factor in the form of HVJ-liposomes (Claim 13 and page 22, lines 6-

18). Morishita et al do not teach a nucleic acid encoding hepatocyte growth factor in the form of HVJ-envelope.

Ramani et al teaches reconstituted Sendai (HVJ) viral envelopes comprising exogenous nucleic acid. Specifically, Ramani et al teach incubation of nucleic acid encoding a reporter gene with the detergent solubilized fraction of HVJ and removal of said detergent resulting in reconstituted viral envelopes containing the nucleic acid encoding a reporter gene (page 11886, col. 2, paragr. 2, lines 1-9). Ramani et al also teach a method of *in vivo* delivery of said reconstituted viral envelopes (page 11888, col. 1, paragr. 3, lines 1-11). Ramani et al do not teach a method of administering a nucleic acid encoding hepatocyte growth factor in the form of HVJ-envelope.

It would have been obvious to an artisan of ordinary skill at the time of the invention to modify the agent and method of Morishita by substituting the HVJ-envelope for HVJ-liposome as a delivery vehicle as taught by Ramani et al with a reasonable expectation of success. An artisan of ordinary skill would have been motivated to use the HVJ-envelope because of the known liposome toxicity and undesirable side effects of HVJ-liposomes as recognized by Ramani et al (page 11889, col. 2, parag. 1, lines 11-20).

Conclusions

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Dowell whose telephone number is 571-272-5540. The examiner can normally be reached on M-F, 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram R. Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Paul Dowell
Art Unit 1632

RAM R. SHUKLA, PH.D.
SUPERVISORY PATENT EXAMINER